



Vesiculobullous diseases affecting the oral cavity: Cicatricial Pemphigoid

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Cicatricial pemphigoid is another of the more commonly diagnosed vesiculobullous diseases of the skin that can also be found within the oral cavity. Previously termed benign mucous membrane pemphigoid, cicatricial pemphigoid is a chronic, subepidermal blistering, scarring, autoimmune disease that mainly affects stratified squamous mucous membranes. The morbidity and mortality rates are lower than those of pemphigus vulgaris however, a prompt and accurate diagnosis of pemphigoid may prevent the blindness that can result from this disease.

Although this disease process can be seen in childhood, cicatricial pemphigoid usually presents initially in the fifth to seventh decade of life and is found more frequently in women. In a study by Vincent, et al., patients were initially referred with a chief complaint of oral pain, "gingivitis," or oral ulceration with the duration of their signs and symptoms averaging 22 months (1). Clinically, the disease is characterized by the formation of bullae which can be found anywhere on the oral mucosa. These bullae rupture, leaving an underlying ulceration. The attached and unattached oral mucosa closely resemble the appearance of desquamative gingivitis which itself can be characterized as an erythematous, denuded and bleeding connective tissue gingival surface presenting in a localized or generalized fashion. This raw and eroded surface finally heals with significant fibrosis and scar formation. The healing process may take as long as 3-4 weeks. A positive Nikolsky sign is present and stress or trauma from mastication or chronic inflammation may contribute to the development of lesions (2). Additionally, it is very uncommon to find an intact oral blister. The etiology of this disease stems from tissue-bound autoantibodies which are directed against one or more components of the basement membrane of mucosal surfaces (3).

The most significant complication of cicatricial pemphigoid, as previously mentioned, is ocular involvement. Ophthalmic referral is essential once the diagnosis has been confirmed as 25% of individuals with oral lesions will have ocular lesions (3). In the presence of cicatricial pemphigoid, the conjunctiva of the eye becomes inflamed and eroded. Healing results in scarring which leads to adhesions referred to as symblepharons. Scarring can ultimately

cause the eyelids to turn inward (termed entropion) which causes the eyelashes to rub against the cornea and globe (termed trichiasis). The eyes then become dry and the cornea produces keratin as a protective mechanism. Blindness usually follows in addition to adhesions between the upper and lower eyelids (3). Additional sites of scarring and stricture formation include the larynx, esophagus and genital mucosa.

Biopsy specimens of cicatricial pemphigoid show a smooth, linear split between the surface epithelium and the underlying connective tissue at the level of the basement membrane thereby allowing blisters to form. A mild infiltrate of chronic inflammatory cells including lymphocytes and plasma cells is noted subjacent to the cleavage sites (1) although this inflammatory component should not be used as a diagnostic discriminator. Direct immunofluorescence studies of fresh tissue show a continuous linear band of immunoglobulin (IgG) and complement (C3) at the basement membrane zone in nearly 90% of affected patients. Like pemphigus vulgaris, tissue must be submitted in Michel's solution to preserve the antigenicity. (Sources of Michel's solution can be obtained by contacting our Department.) The use of frozen tissue is also acceptable although this may be logistically difficult to transport. The use of indirect immunofluorescence is not recommended, as results are not as reliable.

Consultation with a physician may prove helpful and is a must when treating severe cases of pemphigoid, as liver function monitoring may be required. With use of corticosteroids, blistering commonly ceases within 24-48 hours of the start of therapy. Several drug modalities are potentially useful and include anti-inflammatory and immunosuppressive agents. Prednisone is the most useful drug because of its anti-inflammatory and immunosuppressive effects. Rapid resolution can be seen at 0.5 mg/kg daily (4). For patients unresponsive to prednisone, other options remain. Dapsone usually in a dose of 50 mg every 12 hours has been shown to be effective (5). In moderate cases, azathioprine 2-3 mg daily or mycophenolate mofetil 30 mg/kg daily can be used to treat the disease.

Clinically, there are several other conditions that can mimic both pemphigus and pemphigoid and the dentist should at least be familiar with them. These entities often have oral and skin lesions indistinguishable from pemphigus and pemphigoid. The microscopic examination of tissue will usually help differentiate these diseases, as treatment is dependent on an accurate diagnosis. In some cases, direct immunofluorescence will be required.

Paraneoplastic pemphigus is a variant of pemphigus that affects patients who have a known or occult neoplasm, usually lymphoma or chronic lymphocytic leukemia. All patients develop painful mucous membrane ulcerations, multiple blisters and red pruritic skin reactions. The disease course is almost always fatal within two years and is the only form of pemphigus in which internal organs are affected. There is no single optimum therapy for this condition, and referral to a physician is required (4).

The erosive form of lichen planus presents intraorally as an atrophic, erythematous area with central ulceration of varying degree. The periphery of the atrophic region is usually bordered by fine, white radiating striae (3). Patients usually complain of open sores in the mouth and may have characteristic skin lesions often described as purple, pruritic, polygonal papules. A biopsy specimen should be obtained to determine the diagnosis. These are characterized by a band-like infiltrate of lymphocytes of T-cell origin arranged immediately subjacent to the epithelium. The epithelium displays saw-tooth like rete pegs as well as significant blurring of the basement membrane. Treatment usually consists of topical corticosteroids although systemic use is a viable alternative. Lidex gel or ointment (0.05%) (Syntex Laboratories), Temovate gel (0.05%) or ointment (Glaxo Dermatology) or Kenalog in Orabase (0.1%) (Taro Pharmaceuticals) are effective if applied after every meal and at bedtime. Dexamethasone elixir, 0.5 mg/5 ml can be used on a "swish and spit" method for 3-4 minutes 4 times a day. The patient will need to be monitored for iatrogenic candidiasis through mucosal cytologic smears (see Clinical Update Feb 1998).

Linear IgA disease is an uncommon mucocutaneous disorder with up to 50% of affected individuals displaying oral cavity involvement (6). Middle age women are affected most often. Spontaneous manifestations are usually minor and consist of vesicles, painful ulcerations or erosions, and erosive gingival mucositis (7). The sites in the oral cavity include (in order of decreasing frequency) the hard and soft palate, tonsillar pillars, buccal mucosa, tongue, and gingiva (6). Generally, it is difficult to differentiate the clinical manifestations of this disease from those of cicatricial pemphigoid. Biopsy is required for a

diagnosis and topical corticosteroids may be an effective treatment, but systemic therapy is often required (8).

In conclusion, a good understanding of the similarities and differences between pemphigoid and pemphigus is essential to a dental practice. The dentist should be able to develop a differential diagnosis, as well as understand the importance of biopsy to determine the nature of their patient's lesions. Knowledge of how to handle a biopsy specimen and the ability to interpret the pathologic report becomes an important tool in appropriate patient care. Many times the oral cavity is the first site affected and therefore, it is the dentist's responsibility to recognize and initiate treatment of pemphigoid and pemphigus. The therapy provided by the dentist can prevent the potential destructive sequelae of these conditions and more importantly save a person's life.

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